## REMARKS

Claim Amendments

To aid the Examiner and to group independent claims with claims dependent thereon, Claims 16, 21-47, 53, 60, 84, 88, 97-109 and 111-115 have been canceled, and new Claims 122-185 have been added. As described in the following table, many of the new claims correspond to former claims. Support for new claims is also indicated in the table.

| New Claim | Former Claim | Further Support |
|---|---|---|
| 122 | 21 | |
| 123 | 22 | |
| 124 | 23 | |
| 125 | 26, 113 | page 32, lines 1-7 |
| 126 | 26 | page 31, lines 3-18, page 32, lines 1-7 |
| 127 | 24 | page 32, lines 1-7 |
| 128 | 97 | page 32, lines 1-7 |
| 129 | 98 | page 32, lines 1-7 |
| 130 | 113 | |
| 131 | 103 | |
| 132 | 104 | |
| 133 | 103 | page 33, lines 14-20 |
| 134 | 103 | page 33, lines 14-20 |
| 135 | 27 | |
| 136 | 27 | page 33, lines 7-13 |
| 137 | 27 | page 33, lines 7-13 |
| 138 | 27 | page 33, lines 7-13 |
| 139 | 41 | page 32, lines 1-7; Claim 25 as originally filed |
| 140 | 45 | |

| | | |
|---|---|---|
| 141 | 46 | |
| 142 | 44 | |
| 143 | 43 | page 32, lines 1-7 |
| 144 | 101 | page 32, lines 1-7 |
| 145 | 102 | page 32, lines 1-7 |
| 146 | 42 | page 32, lines 1-7; page 35, lines 2-8 |
| 147 | 107 | |
| 148 | 108 | |
| 149 | 107 | page 33, lines 14-20 |
| 150 | 107 | page 33, lines 14-20 |
| 151 | 112 | |
| 152 | 112 | page 33, lines 7-13 |
| 153 | 112 | page 33, lines 7-13 |
| 154 | 112 | page 33, lines 7-13 |
| 155 | 34 | |
| 156 | 38 | |
| 157 | 39 | |
| 158 | 37, 114 | page 32, lines 1-7 |
| 159 | 37 | page 32, lines 1-7 |
| 160 | 35 | page 32, lines 1-7 |
| 161 | 99 | page 32, lines 1-7 |
| 162 | 100 | page 32, lines 1-7 |
| 163 | 114 | |
| 164 | 105 | |
| 165 | 106 | |
| 166 | 105 | page 33, lines 14-20 |
| 167 | 105 | page 33, lines 14-20 |

| | | |
|---|---|---|
| 168 | 111 | |
| 169 | 111 | page 33, lines 7-13 |
| 170 | 111 | page 33, lines 7-13 |
| 171 | 111 | page 33, lines 7-13 |
| 172 | 40 | |
| 173 | 28 | |
| 174 | 29 | |
| 175 | 30 | |
| 176 | 31 | |
| 177 | 32 | |
| 178 | 33 | |
| 179 | 84 | |
| 180 | 88 | |
| 181 | 16 | |
| 182 | 47 | |
| 183 | 53 | |
| 184 | 60 | |
| 185 | 115 | |

The amendments to the claims are supported by the subject application as originally filed. Therefore, this Amendment adds no new matter. All of the former claims have been canceled and new Claims 122-185 have been added. However, as many of the new claims correspond to former claims, the arguments presented below reference both the former claims (now canceled) and corresponding new claims (if appropriate).

Additional remarks addressing the Examiner's comments and rejections are set forth below with reference to the numbered paragraphs of the Office Action.

Paragraph 2. Anticipated Rejoinder of Claims Pursuant to M.P.E.P. § 821.04

Applicants thank the Examiner for his acknowledgment of the request for rejoinder of former Claims 16, 47, 53, 60 and 115 in accordance with M.P.E.P. § 821.04. The Examiner's attention is drawn to the fact that former Claims 16, 47, 53, 60 and 115 have been re-presented as new Claims 181-185, respectively. These withdrawn claims are of the same scope as former independent product Claim 21 (new Claim 122), and therefore, in accordance with M.P.E.P. § 821.04, should be subject to rejoinder upon allowance of product Claim 122.

Paragraph 4. Information Disclosure Statements

Applicants thank the Examiner for his acknowledgment of consideration of the Supplemental Information Disclosure Statement (SIDS) filed on December 30, 2004. A SIDS is being filed concurrently herewith. Entry and acknowledgment of consideration of the SIDS is respectfully requested.

Paragraph 10. Objection to Former Claim 109

Former Claim 109 has been objected to as being a substantial duplicate of former Claim 44. Former Claim 109 has been deleted, thereby obviating the rejection.

Paragraphs 11-13. Rejection of Former Claims 24-26, 35-37, 41-43, 45, 46, 97-102, 113 and 114 Under 35 U.S.C. § 112, First Paragraph

Former Claims 24-26, 35-37, 41-43, 45, 46, 97-102, 113 and 114 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Specifically, the Examiner asserts that while the specification is enabled for an antibody or antigen-binding fragment thereof that:

i) binds mammalian Bonzo and inhibits the binding of a ligand to said Bonzo, wherein said ligand is selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8 (and recited fragments thereof), and

ii) inhibits chemotaxis in response to binding of said ligand to said Bonzo,

the specification does not reasonably enable an antibody or antigen-binding fragment thereof that:

i) binds mammalian Bonzo and inhibits the binding of a ligand to said Bonzo, wherein said ligand is selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8 (and recited fragments thereof), and

ii) inhibits a cellular response selected from the group consisting of proliferation, migration, chemotaxis, secretion, exocytosis, degranulation, inflammatory mediator release, respiratory burst, and $Ca^{2+}$ flux (Office Action, paragraph 11).

The Examiner further asserts that the specification does not enable an antibody or antigen-binding fragment thereof that:

i) binds mammalian Bonzo and inhibits the binding of a ligand to said Bonzo, wherein said ligand is selected from the group consisting of SEQ ID NO:4, SEQ ID NO:6 and SEQ ID NO:8 (and recited fragments thereof), and

ii) inhibits chemotaxis that is not in response to binding of said ligand to said Bonzo. *Id.*

Former Claims 24, 35, 43 and 97-102 (New Claims 127, 160, 143, 128, 129, 161, 162, 144 and 145, Respectively)

In particular, the Examiner asserts that former Claims 24, 35, 43 and 97-102 recite "wherein said antibody or antigen-binding fragments inhibits signal transduction and/or a cellular response", and that such claims are drawn very broadly to inhibiting any signal transduction mechanism or cellular response (Office Action, paragraph 13).

While disagreeing with the Examiner, new Claims 127, 160, 128, 129, 161 and 162 (which correspond to former Claims 24, 35, 97, 98, 99 and 100) recite "wherein said antibody or antigen-binding fragment inhibits chemotaxis induced upon binding of said ligand to said Bonzo in an *in vitro* chemotaxis assay." Similarly, new Claims 143, 144 and 145 (which correspond to former Claims 43, 101 and 102) recite "wherein: i) said ligand-induced cellular response is chemotaxis, and said antibody or antigen-binding fragment inhibits said chemotaxis in an *in vitro* chemotaxis assay." Accordingly, new Claims 127, 160, 143, 128, 129, 161, 162, 144 and 145 are drawn to subject matter that the Examiner acknowledges as being enabled. Reconsideration and withdrawal of the rejection with respect to these claims are respectfully requested.

Former Claims 25 and 36

The Examiner asserts that former Claims 25 and 36 recite "wherein said antibody or antigen-binding fragment inhibits a cellular response selected from the group consisting of proliferation, migration, chemotaxis, secretion, exocytosis, degranulation, inflammatory mediator release and respiratory burst", and that the claims do not require that the cellular response is the result of the binding of the specific ligands that are recited. While disagreeing with the Examiner, former Claims 25 and 36 have been canceled, thereby obviating the rejection with respect to these claims.

Former Claims 26 and 37 (New Claims 125, 126, 158 and 159)

The Examiner asserts that while former Claims 26 and 37 recite "wherein said antibody or antigen-binding fragments inhibits a cellular response, and said cellular response is chemotaxis", they do not require that the cellular response is the result of the binding of the specific ligands that are recited. New Claims 125, 126, 158 and 159 (which correspond to former Claims 26 and 37) recite "wherein said antibody or antigen-binding fragment . . . inhibits chemotaxis induced upon binding of said ligand to said Bonzo", thereby obviating the rejection with respect to these claims.

Former Claim 41 (New Claim 139)

The Examiner asserts that former Claim 41 recites "an antibody or antigen-binding fragment thereof which binds mammalian Bonzo expressed on the membrane of a cell and inhibits a cellular response to binding of a ligand to said Bonzo." The Examiner states that although the claim sets forth that the cellular response is the result of the binding of the specific ligands recited in former Claim 21, that the claim is drawn very broadly to inhibiting any cellular response.

While disagreeing with the Examiner, new Claim 139 recites "[a]n antibody or antigen-binding fragment thereof that binds to mammalian Bonzo expressed on the membrane of a cell and inhibits a ligand-induced cellular response, wherein:

1) said ligand-induced cellular response is selected from the group consisting of:

a) chemotaxis; and

b) a transient increase in the concentration of cytosolic free calcium ($[Ca^{2+}]_i$)."

Inhibition of such ligand-induced cellular responses are supported and enabled by the specification. With respect to inhibiting chemotaxis, the specification describes chemotaxis assays (see, e.g., Specification, page 23, line 28 to page 25, line 2, and Example (page 64, line 1 *et seq.*)), and exemplifies inhibition of SExCkine-induced chemotaxis of cytokine-induced killer (CIK) cells, which express Bonzo, by the anti-Bonzo monoclonal antibody mAb 7F3 (Specification, page 71, lines 7-12 and Figure 21).

With respect to inhibiting calcium flux, the specification teaches that ligand (e.g., SExCkine) binding to Bonzo results in a transient increase in the concentration of cytosolic free calcium ($[Ca^{2+}]_i$) (see, e.g., Specification, page 32, lines 1-7). The specification further teaches that functional assays, such as a calcium flux assay, can be used to determine whether an agent modulates one or more functions of Bonzo (Specification, page 23, lines 19-27). In addition, the specification cites to particular references, such as Hesselgesser *et al.* and WO 98/02151, which describe various assays that can be used to analyze chemokine receptor (e.g., Bonzo) function (Specification, page 23, lines 19-27). For example, Hesselgesser *et al.* describe the use of an assay to measure inhibition of MIP-1α-induced $Ca^{2+}$ flux by 4-hydroxypiperidine analogs (Hesselgesser *et al., J. Biol. Chem.* 273(25):15687-92 (1998); page 15688, right-hand column, section entitled "Cytosolic $Ca^{2+}$ Measurements in HEK Cells" and FIGS. 4 and 5; cited as Reference AR7 in Supplemental Information Disclosure Statement being filed concurrently herewith). Thus, in contrast to the Examiner's assertion (Office Action, page 6, lines 17-21), the specification does teach that ligand (e.g., SExCkine) binding to Bonzo results in an increase in the concentration of cytosolic free calcium (see, e.g., page 32, lines 1-7).

Further evidence that ligand (e.g., SExCkine) binding to Bonzo results in an increase in the concentration of cytosolic free calcium, as taught in the specification, is provided by U.S. Publication No. 20030165995, published on September 4, 2003 (U.S. Application No. 10/174,293; "the '293 Application"), which is a continuation-in-part application claiming priority to the subject application. The '293 Application teaches and exemplifies that addition of recombinant SExCkine (consisting of the entire predicted extracellular domain of SExCkine,

amino acid residues 1 to 202) to transfected L1.2 cells that expressed Bonzo resulted in an increase in intracellular calcium (see Example 8 of Published Application No. 20030165995, which is cited as Reference AK in the Supplemental Information Disclosure Statement being filed concurrently herewith). The teachings and exemplification of the '293 Application (U.S. Publication No. 20030165995) demonstrate that the teachings and assertions in the subject application with respect to $Ca^{2+}$ flux upon binding of ligand to Bonzo, are in fact true. Therefore, in view of the teachings in the specification and the skill in the art, it is clear that the claimed antibodies and antigen-binding fragments are enabled. Accordingly, reconsideration and withdrawal of the rejection with respect to this claim are respectfully requested.

Former Claim 42 (New Claim 146)

The Examiner asserts that former Claim 42 (new Claim 146) recites "an antibody or antigen-binding fragment thereof which binds mammalian Bonzo expressed on the membrane of a cell and inhibits a cellular response to binding of a ligand to said Bonzo, wherein said cellular response is selected from the group consisting of $Ca^{2+}$ flux, chemotaxis, exocytosis and respiratory burst", and that the specification does not teach a commensurate number of the claimed cellular responses that are inhibited by such antibodies (Office Action, page 6, lines 11-15 and sentence bridging pages 6 and 7). While disagreeing with the Examiner, new Claim 146 recites "[t]he antibody or antigen-binding fragment . . . wherein said ligand-induced cellular response is a transient increase in the concentration of cytosolic free calcium ($[Ca^{2+}]_i$)." As described above (see section entitled "Former Claim 41 (New Claim 139)"), antibodies and antigen-binding fragments that inhibit calcium flux are enabled by the Specification. Indeed, corroboration of the teachings of the subject application are provided by the '293 Application (U.S. Publication No. 20030165995), which exemplifies a transient increase in the concentration of cytosolic free calcium upon binding of SExCkine to Bonzo. Accordingly, reconsideration and withdrawal of the rejection with respect to this claim are respectfully requested.

Former Claims 113 and 114 (New Claims 125, 130, 158 and 163)

The Examiner asserts that former Claims 113 and 114 recite "wherein said antibody or antigen-binding fragment inhibits transient increase in the concentration of cytosolic free calcium induced upon binding of ligand to said Bonzo", and that the specification has not taught that binding of said ligands results in an increase in the concentration of cytosolic free calcium. As described above (see section entitled "Former Claim 41 (New Claim 139)"), and in contrast to the Examiner's assertion, the specification does teach that ligand (e.g., SExCkine) binding to Bonzo results in a transient increase in the concentration of cytosolic free calcium $[Ca^{2+}]_i$) (see, e.g., Specification, page 32, lines 1-7). Further, corroboration of the teachings of the subject application are provided by the '293 Application (U.S. Publication No. 20030165995), which exemplifies a transient increase in the concentration of cytosolic free calcium upon binding of SExCkine to Bonzo. Accordingly, reconsideration and withdrawal of the rejection with respect to this claim are respectfully requested.

Paragraphs 14-16. Rejection of Former Claims 24, 35, 43 and 97-102 Under 35 U.S.C. § 112, Second Paragraph

Former Claims 24, 35, 43 and 97-102 (new Claims 127, 160, 143, 128, 129, 161, 162, 144 and 145, respectively) are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention (Office Action, paragraph 15). In particular, the Examiner asserts that the recitation of "signal transduction and/or a cellular response" and "in an *in vitro* chemotaxis assay" in former Claims 25, 35, 43 and 97-102 make it unclear as to what is encompassed by the phrase "signal transduction and/or a cellular response".

New Claims 127, 160, 143, 128, 129, 161, 162, 144 and 145 (which correspond to the rejected former claims) do not recite "signal transduction and/or a cellular response", thereby obviating the rejection with respect to these claims. Accordingly, reconsideration and withdrawal of the rejection with respect to these claims are respectfully requested.

Paragraphs 17-18. Rejection of Former Claims 21-26, 34-46, 97-102, 109, 113 and 114 Under 35 U.S.C. § 102(b)

The Examiner states that former Claims 21-26, 34-46, 97-102, 109, 113 and 114 (which correspond to new Claims 122-130, 139-146 and 155-163, although not in that same order (see Table)) remain rejected under 35 U.S.C. § 102(b) as being anticipated by Farber *et al.* (WO 98/44098; Reference AP, of record) for the reasons set forth in the previous Office Action (Office action, paragraph 17). In particular, the Examiner states the following:

1) That Applicants' argument that Farber *et al.* only suggest, but do not actually teach or exemplify any particular anti-STRL33 antibodies that are capable of blocking membrane fusion between HIV and target cells, is not persuasive because it is not necessary that Farber *et al.* provide working examples (Office Action, paragraph 18).

2) That, although the references cited by Applicants (Lee *et al.* (*J. Biol. Chem., 274(14)*:9617-9626 (1999), Reference AV6, of record); Wu#1 (Wu *et al.*, *J. Exp. Med., 185(9)*:1681-1691 (1997), Reference AT3, of record); and Wu#2 (Wu *et al.*, *J. Exp. Med., 186(8)*:1373-1381 (1997), Reference AW6, of record)) teach that certain monoclonal antibodies that bind CCR5 (another chemokine receptor that is a coreceptor for HIV-1 cellular entry) exhibit differences in their ability to inhibit chemokine binding and HIV-1 binding, these references do not show that antibodies that block HIV-1 binding would necessarily have no effect on chemokine binding. *Id.* (emphasis added).

3) That the antibodies taught by Farber *et al.*, which includes antibodies that bind STRL33 and inhibit binding of HIV-1 to Bonzo, would, in the absence of evidence to the contrary, inhibit binding of any other ligand to Bonzo (Office Action, page 9, lines 3-5).

4) That "[s]ince the Office does not have the facilities for examining and comparing Applicants' antibody with the antibodies of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the antibody of the prior art does not possess the

same material structural and functional characteristics of the claimed antibody) (Office Action, page 9, lines 5-9).

Legal Standard For Inherent Anticipation

A claim is anticipated under 35 U.S.C. § 102 only if "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil of Cal.*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987) (see also, M.P.E.P. § 2131, pp. 2100-73 *et seq.*, 8th Ed., Latest Rev., May 2004). "Inherency, however, may not be established by probabilities or possibilities; [t]he mere fact that a certain thing may result from a given set of circumstances is not sufficient [to establish inherency]." *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1951 (Fed. Cir. 1999) (quoting *In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981)). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates." *MEHL/Biophile Intl. Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999) (quoting *In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986)).

In contrast to the Examiner's statement, Farber *et al.* does not inherently anticipate the claimed antibodies and antigen-binding fragments. The arguments presented in the Amendment filed on December 28, 2004 are incorporated herein in their entirety.

In Applicants' previous Amendment filed on December 28, 2004, the teachings of particular references, namely Lee *et al.*, Wu#1 and Wu#2, were described in detail. As stated by the Examiner, these references teach that particular monoclonal antibodies that bind CCR5, another chemokine receptor, which, like Bonzo, is a coreceptor for HIV-1 cellular entry, exhibit differential effects on binding of HIV-1 Env and binding of chemokine (Office Action, page 8, lines 8-11). Notwithstanding these teachings, the Examiner states that these references do not show that antibodies that block HIV-1 binding would necessarily have no effect on chemokine binding. (Office Action, page 8, lines 18-20, emphasis added). The Examiner further states that Lee *et al.* teach an antibody, 2D7, that inhibits both chemokine binding and HIV-1 envelope binding, and that Farber *et al.* not only disclose an antibody that inhibits binding of HIV-1 to

Bonzo (STRL33), but also disclose antibodies that bind different epitopic specificities (Office Action, page 8, line 20 to page 9, line 2). The Examiner concludes that the antibodies taught by Farber *et al.*, which include antibodies that bind STRL33 and inhibit binding of HIV-1 to Bonzo, would, in the absence of evidence to the contrary, inhibit binding of any other ligand to Bonzo.

First, it is not Applicants' burden to demonstrate that the prophetic antibody disclosed by Farber *et al.* would necessarily have no effect on chemokine binding. Instead, under the appropriate legal standard for inherent anticipation, the antibodies disclosed by Farber *et al.* can only inherently anticipate Applicants' claimed antibodies if they necessarily and inevitably possess the claimed binding and functional properties (e.g., if they necessarily and inevitably bind to mammalian Bonzo and inhibit the binding of the recited ligands, and/or inhibit the recited ligand-induced cellular responses). Clearly, the acknowledged teachings of Lee *et al.*, Wu#1 and Wu#2 demonstrate that antibodies that bind a known chemokine receptor that also functions as an HIV-1 co-receptor, have differential effects on binding of HIV env and binding of chemokine. Accordingly, and in the absence of any further evidence, there is no credible scientific reasoning to support the Examiner's opinion that the postulated antibodies of Farber *et al.* would necessarily and inevitably inhibit binding of the recited ligands to Bonzo and/or inhibit the recited ligand-induced cellular responses.

Further evidence that the postulated antibodies disclosed by Farber *et al.* do not necessarily and inevitably inhibit chemokine binding and/or function is provided by Doranz *et al.* (Doranz *et al.*, *J. Virol. 73(4)*:2752-61 (1999); cited as Reference AZ6 in the Supplemental Information Disclosure Statement being filed concurrently herewith). Doranz *et al.* teach that several mutants of CXCR4, another chemokine receptor that is a coreceptor for HIV, are unable to bind the chemokine ligand SDF-1, but are still able to support HIV-1 infection (Doranz *et al.*, abstract). Like the teachings of Lee *et al.*, Wu#1 and Wu#2, the teachings of Doranz *et al.* demonstrate that there are regions of the chemokine receptor that are important for HIV-1 entry that differ from those regions that are important for chemokine binding and/or activity. In view of these teachings and the knowledge in the art that the ability of these two chemokine receptors (CCR5, CXCR4) to act as coreceptors for HIV entry is independent of their ability to bind chemokines and signal in response, it is clear that the postulated antibodies of Farber *et al.*,

which include antibodies that bind Bonzo and block membrane fusion between HIV and target cells, would not necessarily and inevitably block chemokine binding and/or function.

The antibodies postulated by Farber *et al.* represent a genus that encompasses antibodies that bind Bonzo and block membrane fusion between HIV and target cells. For a teaching of such a postulated genus to inherently anticipate the claimed invention, the genus of antibodies must necessarily and inevitably possess the claimed functional properties (i.e., all species within the genus must possess the claimed functional properties). For inherent anticipation, it is not enough that one could envision particular species of the genus (e.g., particular antibodies) that bind to a receptor (e.g., Bonzo) and inhibit binding of particular ligands (e.g., the ligands recited in the claims) and/or inhibit particular functions (e.g., the ligand-induced cellular responses recited in the claims). Rather, all species must possess the claimed binding and functional properties. Otherwise, the prior art teaching is not of a product that necessarily and inevitably possesses the properties of the claimed product. Clearly, in view of the teachings of Lee *et al.*, Wu#1, Wu#2 and Doranz *et al.*, it is not the case that all antibodies that bind Bonzo and block membrane fusion between HIV and target cells will necessarily and inevitably possess the claimed properties of binding to Bonzo and inhibiting binding of the recited ligands and/or inhibiting the recited ligand-induced cellular responses. Similarly, the disclosure by Farber *et al.* of a second genus of antibodies, namely antibodies of different epitopic specificities, which the Examiner references (Office Action, sentence bridging pages 8 and 9), also fails to inherently anticipate the claimed invention, because not all members of this genus necessarily and inevitably bind to Bonzo and inhibit binding of the recited ligands and/or inhibit the recited ligand-induced cellular responses.

The U.S.P.T.O. Has Not Properly Shifted the Burden to Applicant

In the Office Action, the Examiner cites In re Best, 562 F.2d 1252, 1253, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977) and Ex parte Gray, 10 U.S.P.Q. 2d 1922, 1923 (Bd. Pat. App. & Int.), and states that "[s]ince the Office does not have the facilities for examining and comparing Applicants antibody with the antibodies of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the antibody of the prior art does not possess the same material structural and functional

characteristics of the claimed antibody) (Office Action, page 9, lines 5-9). However, the facts presented in the cited cases differ from the facts relating to the subject application. For example, in In re Best, the applicant claimed a process for preparing a hydrolytically-stable zeolitic aluminosilicate (zeolite), which included a step of cooling the steamed zeolite at a rate sufficiently rapid such that the cooled zeolite exhibited a particular X-ray diffraction pattern. In re Best, 562 F.2d 1252, 1253 (C.C.P.A. 1977). The prior art taught a method for producing a zeolite composition that included all of the limitations of the claimed process, but did not disclose the functionally expressed rate of cooling. Id. at 1254. However, because the process taught by the prior art reference would necessarily be cooled to facilitate subsequent handling, and the applicant failed to present data comparing the X-ray diffraction patterns of the zeolites produced using the claimed and prior art processes, the C.C.P.A. held that the applicant's claimed process was inherently anticipated. Id. at 432-433. Importantly, and in contrast to the facts relating to the subject application, in In re Best the claimed and prior art products, and the methods used for their production, were identical or substantially identical. As stated by the court:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product.

Id. at 1255, emphasis added.

Unlike the prior art method described in In re Best, the prior art antibodies disclosed by Farber *et al.* are not identical or substantially identical to the claimed antibodies and antigen-binding fragments. In particular, and as described, the postulated antibodies disclosed by Farber *et al.* are a genus of antibodies, not all of which necessarily and inevitably possess the claimed properties of binding to Bonzo and inhibiting binding of the recited ligands and/or inhibiting the recited ligand-induced cellular responses. Given that the postulated antibodies disclosed by Farber *et al.* are not identical or substantially identical to the claimed antibodies and antigen-binding fragments, it is improper for the U.S.P.T.O. to require Applicants to prove that the antibodies disclosed by Farber *et al.* do not necessarily or inherently possess the characteristics of the claimed antibodies and antigen-binding fragments.

In addition, as described in the Amendment filed on December 24, 2004, Farber *et al.* do not actually teach or exemplify any particular anti-STRL33 antibodies that are capable of blocking membrane fusion between HIV and target cells; instead they merely suggest that such an antibody might be produced. The Examiner states that it is not necessary for Farber *et al.* to provide working examples. Because Farber *et al.* do not disclose an existing antibody, neither the U.S.P.T.O. nor Applicants have the ability to physically test the antibody of Farber *et al.* to determine whether it possesses the claimed properties.

Therefore, in view of the foregoing, reconsideration and withdrawal of the rejection are respectfully requested.

Paragraphs 19-20. Rejection of Former Claim 84 Under 35 U.S.C. § 103(a)

Former Claim 84 (new Claim 179) is rejected under 35 U.S.C. § 103(a) as being obvious in view of Farber *et al.* (WO 98/44098; cited as Reference AP in IDS) in further view of Jardieu *et al.* (U.S. Patent No. 6,037,454; cited in Form PTO-892 accompanying Office Action dated 09/22/03). The Examiner states that Applicants' arguments filed in the previous Amendment have been considered but have not been deemed persuasive, and that the rejection is maintained for the reasons of record.

In the previous Office Action dated July 28, 2004, the Examiner asserted that although Farber *et al.* do not teach an antibody to Bonzo in a test kit comprising ancillary reagents suitable for detecting the antibody-Bonzo complex, that Jardieu *et al.* teach antibodies to another cell surface receptor, CD11A, which may be packaged in a kit with ancillary agents for detection. (Office Action dated July 28, 2004, pages 9 and 10, paragraphs 39, 40 and 41). According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the anti-Bonzo antibody taught by Farber *et al.* with one or more ancillary detection reagents, as taught by Jardieu *et al.* (Office Action dated July 28, 2004, page 10, paragraph 42). The Examiner further asserted that the person of ordinary skill in the art would have been motivated to produce the antibody in a kit as a matter of convenience, as taught by Jardieu *et al.*, and that in view of the teachings of Farber *et al.* of the anti-Bonzo antibody and Jardieu *et al.* of numerous ancillary reagents, that one would have had a reasonable expectation of formulating the antibody in a kit. (Office Action dated July 28, 2004, page 10, paragraph 42).

As described above, Farber *et al.* does not inherently teach or suggest the claimed antibodies and antigen-binding fragments. Further, the teachings of Jardieu *et al.* do not teach or suggest the claimed antibodies and antigen-binding fragments. Accordingly, Claim 84 is not obvious over the cited combination, because neither reference, alone or in combination, teaches or suggests, or provides a reasonable expectation of success in producing, the claimed antibodies.

Indication of Allowable Subject Matter

In the Office Action, the Examiner states that former Claims 27, 88, 103-108, 111 and 112 (which correspond to new Claims 131-138, 147-154, 164-171 and 180, although not in that order) are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and intervening claims (Office Action, paragraph 21). For the reasons described above, it is believed that all claims are in condition for allowance.

The Examiner further states that former Claims 28-33 (new Claims 173-178) remain allowable as the prior art does not teach or suggest the particular species of antibodies and cell lines producing said antibodies.

## CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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